UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/601,171	07/28/2000	Michael Buschle	0652.2100000	6961

26111 7590 05/23/2003

STERNE, KESSLER, GOLDSTEIN & FOX PLLC
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER
NAVARRO, ALBERT MARK

ART UNIT	PAPER NUMBER
1645	13

DATE MAILED: 05/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/601,171	Applicant(s) Buschle et al
	Examiner Mark Navarro	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *17, 24, 25, and 28-47* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *17, 24, 25, and 28-47* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's amendment filed February 12, 2003 (Paper Number 12) has been received and entered. Claims 18-23 and 26-27 have been canceled and new claims 35-47 have been added, consequently claims 17, 24-25, and 28-47 are pending in the instant application.

SEQUENCE LISTING

Applicant's submission of a computer readable copy of the sequences on February 12, 2003 (Paper Number 12) has been received and entered.

Claim Rejections - 35 USC § 112

1. The rejection of claim 32 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained.

Applicants are asserting that cancer vaccine therapy has shown remarkable success in the treatment of lymphoma, leading to complete remission in one study. Applicants further assert that the example in the captioned application that a significant percentage of mice injected with a vaccine of the invention remained tumor free after challenge with tumor cells relative to mice

injected with a control vaccine. Applicants arguments have been fully considered but are not found to be fully persuasive.

Applicants arguments are not found to be fully persuasive in view of the teachings of Yamana *et al.*

Yamana *et al* report of the identification of **several** possible tumor antigens. Yamana *et al* further set forth that recent studies have reported that many tumors escape from CTL recognition by downregulation of HLA class I expression. In other words many tumor antigens have been identified, very few have proven to have any beneficial use. The examiner has not taken the position that each and every tumor antigen will prove futile. However the claims are not limited to any particular antigen, and therefore encompass myriads of antigens, the majority of which, have proven ineffective. Consequently, one of skill in the art would be forced into undue experimentation to identify which of the multitude of antigens would rise to the level of "trigger an immunoprotective response in the host vaccinated." In re Wright, 999F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

The claim is directed to a vaccine wherein the peptide is derived from a tumor antigen.

Yamana *et al* (Japanese Journal of Cancer and Chemotherapy, Sept. 2000, Vol. 27, No. 10, pp 1477-1488) set forth of the recent identification of several possible tumor antigens. Yamana *et al* further set forth that recent studies have reported that many tumors escape from

CTL recognition by downregulation of HLA class I expression. Moreover, most cancer cells produce suppressor agents against the immune system. Yamana *et al* conclude that "we must resolve major problems to produce successful cancer vaccine therapy soon."

A vaccine "must by definition trigger an immunoprotective response in the host vaccinated; mere antigenic response is not enough." In re Wright, 999 F.2d 1557,1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

Given that successful cancer vaccine therapy still has to resolve major problems as evidenced by the teaching of Yamana *et al*, one of skill in the art would be forced into excessive experimentation to practice the broadly claimed invention in view of the lack of working examples, lack of guidance, and lack of success of others in the art.

For reasons of record in Paper Number 11, as well as the reasons set forth above, this rejection is maintained.

2. The rejection of claims 17-34 under 35 U.S.C. 112, second paragraph, as being vague and indefinite in the recitation of "low concentration of inorganic salts." is withdrawn in view of Applicants amendment.

3. The rejection of claims 17-34 under 35 U.S.C. 112, second paragraph, as being vague and indefinite in the recitation of "highly purified." is withdrawn in view of Applicants amendment.

4. The rejection of claims 18-19 under 35 U.S.C. 112, second paragraph, as being vague and indefinite in the recitation of a "substantially free." is withdrawn.

5. The rejection of claims 25 under 35 U.S.C. 112, second paragraph, as being vague and indefinite in the recitation of "slightly hypotonic" is withdrawn.

6. The rejection of claim 32 under 35 U.S.C. 112, second paragraph, as being vague and indefinite in the use of the phrase "derived from." is maintained.

Applicants are asserting that the term "derived from" is supported in the specification and can be for example, fragments and cellular breakdown products of antigenic proteins.

Applicants arguments have been fully considered but are not found to be persuasive.

Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Consequently, the metes and bounds of the term "derived" remain unclear.

It is unclear if the antigens are undergoing any kind of chemical modification as implied by the recitation of "derived from." Since it is unclear how the antigens are to be derived as referred to in the claims, there is no way for the person of skill in the art to ascribe a discrete and identifiable definition to said phrase.

For reasons of record in Paper Number 11, as well as the reasons set forth above this rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

7. The rejection of Claims 17, 24-25, 28-32 under 35 U.S.C. 102(e) as being anticipated by Hauser *et al* is maintained. Additionally this rejection is applied to newly added claims 35-36, 42 and 46-47.

Applicants are asserting that the composition disclosed by the '468 patent is not substantially free from inorganic salt ions as required by amended claim 17 of the captioned application. Applicants point to the '468 patent at column 3, lines 46-54, which reports the use of phosphate buffer and contend therefore that the '468 patent added inorganic ions.

Applicants arguments have been fully considered but are not found to be fully persuasive.

Applicants arguments are not found to be fully persuasive in view of the disclosure of Hauser *et al.*

Applicants assert that the '468 patent recites that "MPL does not aggregate in the presence of phosphate buffer, *as may happen during formulation without them.*" However, Applicants attention is directed to the claims of the '468 patent. No inorganic ions are recited in the claims, accordingly their presence is not a requirement, and therefore, the instant claims remain anticipated. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The claims are directed to a vaccine containing one or more synthetic or highly purified natural peptides as antigen(s) as well as one or more adjuvants, characterized in that it is present as a solution or emulsion which is substantially free from inorganic salt ions.

Hauser *et al* (U.S. Patent Number 5,776,468) disclose of a vaccine comprising a purified peptide antigen in combination with an adjuvant in a solution. Hauser *et al* further disclose of the vaccine containing sorbitol. (See claims).

It is noted that the claims also recite that the solution is "substantially free from inorganic salt ions." Given that the claims of U.S. Patent Number 5,766,468, do not recite the presence of any inorganic salt ions, the composition disclosed by Hauser *et al* is deemed to be "substantially free from inorganic salt ions."

Since the Patent office does not have the facilities for examining and comparing applicants' product with the product of the prior art reference, the burden is on applicants to show an unobvious distinction between the material structural and functional characteristics of the claimed product and the product of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

8. The rejection of claims 17-34 under 35 U.S.C. 102(b) as being anticipated by Schmidt *et al* is withdrawn in view of Applicants amendment.

The following new grounds of rejection are applied to the amended claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 17, 24-25, and 28-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hauser *et al* and Schmidt *et al* in view of Chazono *et al* and McAleer *et al* and Loudon *et al* and McAleer *et al*.

The claims are directed to a vaccine containing one or more synthetic or purified natural peptides or proteins as antigens as well as one or more adjuvants, characterized in that it is

present as a solution or emulsion which is substantially free from inorganic salt ions and comprises maltose, fructose, galactose, saccharose, sugar alcohol, lipid or combinations thereof.

The teachings of Hauser *et al* and Schmidt *et al* have been previously set forth.

Neither Hauser *et al* nor Schmidt *et al* teach of maltose, fructose, galactose, saccharose, or mannitol.

Chazono *et al* (US Patent 4,849,358) teach of customary stabilizing agents for use in vaccines to include fructose or galactose. (See summary).

McAleer *et al* (US Patent 4,338,335) teach of customary stabilizing agents for use in vaccines to include sorbitol or maltose. (See claims).

Loudon *et al* (US Patent 6,258,362) teach of customary stabilizing agents for use in vaccines to include saccharose. (See summary).

McAleer *et al* (US Patent 4,147,772) teach of customary stabilizing agents for use in vaccines to include mannitol. (See claims).

Given that 1) Hauser *et al* has taught of vaccines containing one or more synthetic or purified natural peptides as antigens as well as one or more adjuvants, that is present as a solution which is substantially free from inorganic salt ions, and that 2) Schmidt *et al* have taught of the advantages of polyarginine as an adjuvant, and that 3) each of Chazono *et al*, McAleer *et al*, Loudon *et al* and McAleer *et al* have taught of the advantages of adding stabilizers to a vaccine composition, and specifically fructose, galactose, maltose, saccharose and mannitol, it would have

been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have taken the vaccine as taught by Hauser *et al* and incorporated polyarginine as an adjuvant as taught by Schmidt *et al* and to further have incorporated well known stabilizers such as fructose, galactose, maltose, saccharose or mannitol, as taught by Chazono *et al*, McAleer *et al*, Loudon *et al* and McAleer. One would have been motivated to add a stabilizer in view of the teachings of Chazono *et al*, McAleer *et al*, Loudon *et al* and McAleer that stabilizers increase the viable storage life of the resulting composition.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro, whose telephone number is (703) 306-3225. The examiner can be reached on Monday - Thursday from 8:00 AM - 6:00 PM. The examiner can be reached on alternate Fridays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Lynette Smith can be reached at (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 1645 by facsimile transmission. Papers should by faxed to Group 1645 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the official Gazette 1096 OG 30 (November 15, 1989). The CMI Fax Center number is (703) 308-4242.

Mark Navarro

Primary Examiner

May 19, 2003